# COMPARATIVE EVALUATION OF VECURONIUM PANCURONIUM AND GALLAMINE ON CARDIOVASCULAR SYSTEM

## **THESIS**

FOR

# DOCTOR OF MEDICINE

( ANAESTHESIOLOGY )







BUNDELKHAND UNIVERSITY JHANSI (U. P.)

#### <u>GERTIFICATE</u>

Certified that the work entitled \*COMPARATIVE EVALUATION OF VECURONIUM PANCURONIUM AND GALLAMINE ON CARDIOVASCULAR SYSTEM" which is being submitted as a thesis for N.D. (Anaesthesiology) was conducted by Dr. Mahendra Kumar himself in the department of Anaesthesiology, N.L.B. Nedical College, Jhansi.

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#### ACKNONLEDGEMENTS

Word, in fact can not substitute for the feeling of gratitude, I have towards all who have helped me in this work.

There can be no greater opportunity than this to express my profound sense of gratitude to my esteemed and exalted guide and teacher Dr. A.K. Gurwara, M.S.,D.A., Reader in Department of Ansesthesiology, M.L.B. Medical College, Jhansi, who with his unfathomed knowledge and untiring zest for work guided me unflinchingly throughout this work. The present work has been possible because of his wise counsel, firm initiatives, timely and constructive criticism and valuable advice, which I have had the good fortune to receive.

I must express my deepest gratitude to my revered teacher Dr. P. Sahi, M.D., D.A., Lecturer, Department of Anaesthesiology, M.L.B. Medical College, Jhansi, for his excellent guidance, supervision and unlimited help at every juncture, his constructive and meticulous suggestions have gone a long way in the accomplishment of this work.

I acknowledge with sincere thanks, the affectionate nature, heartening words and constant encouragement of Dr. U.C. Sharma, M.D., D.A., Professor and Head of the Department of Anaesthesiology, M.L.B. Medical College, Jhansi, which has provided me the confidence and enthusiasm so essentially vital for successful accomplishment of such a study.

I am highly obliged and thankful to all of my senior staff especially -

- 1. Dr. D.D. Verma.
  M.D., D.A.,
  Lecturer,
  Department of Anaesthesiology,
  M.L.B. Medical College, Jhansi.

who as a perpetual source of inspiration and knewledge bestowed upon me with remarkable generosity and benevolence.

I am highly obliged and thankful to our staff members of the Department of Anaesthesiology, whose encouragement and constant help make this work possible.

I shall always remain indebted to my parents, wife brothers and sisters for their unaccountable pain and sacrifice and their persistent inspiration which enable me to perform this work successfully. I most humbly take the liberty of dedicating this work to my parents.

I should appreciate the helping and co-operating attitude of my department workers - Mr. Zaheer Hasan (Clerk), Mr. Om Prakash (Technician) Mr. OM Prakash Yadav (department boy), Department of Anaesthesiology, M.L.B. Medical College, Jhansi, who helped me by all means time to time.

I am also thankful to Mr. K.C. Sharms for bringing out the work in representable form by his excellent ability of preparing type scripts.

Lastly, I am highly obliged to those patients who became the subjects of this work.

Date: 1.8.91

( MAHENDRA KUMAR )

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INTRODUCTION

constitutes the tried of requirements for general ansesthesis to provide satisfactory operative conditions. Ever since Griffith et al. used curare for clinical ansesthesis in 1942, newer muscle relaxants had been introduced from time to time with certain advantages over the existing muscle relaxants.

the anaesthetic practice. It become possible to produce active muscular relaxation without unwanted depression of various systemes with the rapid advancement in the field of anaesthesiology. Muscle relaxants now have been used in millions of surgical patients for a variety of surgical procedures. However the muscle relaxants themselves have some undesirable side effects. The effect on heart and peripheral circulation occurbecause of stimulation or inhibition of nicotinic receptors; in autonomic gangelia or on muscarinic receptors: in the sinus node of the heart or as result of systemic histamine release. These autonomic action may result in changes in heart rate and rhythm, peripheral vescular resistance and venous capacitance.

limiting its use in certain situations. The accompanying rise in intragastric pressure, painful muscle stiffness due to fasiculation, hyperkalemia, cardiac arrthymies and even cardiac arrest have been reported with summethonium in burns and traumas cases (Mazze 1969). Breakdown products of summithonium tend to accumulate and have unwanted neuromuscular blocking property. These effects are not easily antagonised under these circumstances, use of a nondepolarising relaxants should be preferable for muscular relaxation which have a rapid enset and a relatively short duration of action.

The synthatic muscle relaxant gallamine triethiodide was first described in 1947 (Boret, Depierre and Lestrange) and introduced in to ansesthetic practice in the following year (Huguendard and Boul 1948). Although its primary action at the myoneural junction has been carefully evaluated. The occurence of circulatory changes following the use of gallamine triethiodide in anaesthesis was first reported in 1949 (Larnoureux Bourge Cavardin). These authors observed that techycordia was an almost unverying sequel to its

administration. It produced hypertension, increases cardiac out put and left ventricular work in anaesthetized humanse (Smith and Whitcher 1967). It is reported to produce ventricular arrathymias in 56% of patients who recieve the drug during cyclopropane anaesthesia (Wats and Prescott 1965). For producing complete apones, it is used in the dose of 2mg/kg body weight by intravenous route, the duration of action is about 20-25 min. About 30% administered dose is excreted in kidney so should not be used in patients with renal disorders the remaining is antagonised by neostigmine and atropine.

One of the most fascinating contributions to medicine is the progress made in correlating chemical structure of drugs to their site and mode of action. Muscle relamants represent a supreme example of success in this field, while investigating a series of aminosteroids. Hewitt and Savagein 1964 observed that when an acetyleheline like group was added to these triologically active compounds, some neuromuscular (N-M) blocking properties were obtained. One such compound, Pancuronium bromide appeared to be very effective (N-M) blocking agent without evidence

of amy steroid activity. A large number of studies by various workers has resulted in the safe clinical introduction of this useful drug.

in 1967 by Baired and Reed, and the advantages claimed were the absonce of side effects, less histamine releasings activity (Loh 1970) and a weaker neurom ganglion blocking action (Calton 1972). It did not appear to preduced bronchospass or hypotension, others worker have reported a rise in blood pressure (Loh 1970, Kelmann and Kennedy 1970).

for new nondepolarizing relaxants of shorter duration, less quantative propensity, and fewer side effects then presently available drugs. New several new substances which do possess the desirable properties hypothetized above have been produced and are in various stages of clinical trial. These new relexants will no doubt changes our patterns of practice by improving the safety and verstility of clinical relaxation.

Vecuronium is an excellent example of how an opporently minor molecular change may result in aignificant alteration of pharmacologic activity.

Chemically the drug is simlary Fancuronium without the quaternizing methylo group in the 2-piperidine substitution (Fahey et al 1981), hence the trade name Norouron. Vecuronium is therefore a Momoquatermary substance (although the tertiary amine at position-2 is probably protonated in the physiologic pit range). This seemingly minor chemical difference is responsible for all of the considerable pharmacologic differences between Vecuronium and Pancuronium. The absence of this methyla group reduces the acetyle-choline like character of the molecule in the area of ring "A" of the steroid nucleus, there by lessening its vagolytic property without loss of neuromuscular blocking activity. Increased liver metabolic may be one reason for the shorter duration of action of Vecuronium compared to Pencuronium.

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Veguronium is one of several new relaxants currently undergoing clinical evaluation which appear to be actively metabolized within the body to relatively inactive derivatives. Vecuronium therefore have shorter duration of action and less cumulative effect than current drugs, as well as being less depends on the kidney for elimination (Agoston et al 1980, Marshall et al. 1980) and the residual is easily reversed by Recatigmine.

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REVIEW OF LITERATURE

Kennedy et al. (1968) studied the cardiovascular effects of Gellamine triethiodide in 14 petients undergoing surgery. They observed that after Gallamine triethiodide, an increase in heart rate was found consistently. The tachycardia was marked both in degree and rapidity of onset. The average increase in heart rate was 40%. Tachycardis was said to occur however with small the desage of Gallamine and has long been believed to result from blockade of the muscarinic effects of Acetylecholine librated from the post ganglionic vagal nerve endings. In this action the drug resembles atropine although it is much weaker (Laity and Garg 1962). There was no evidence of general sympathetic stimulation and the effect on preganglionic sympathetic nerves are minimal (Miller and Biscoe 1965). A direct stimulant effect on intra cardiac Beta receptores has recently been demonstrated but the extent to which the tachycardia results from this mechanism has not yet been decided. Elevation of Mean Arterial Pressure was found in all patients. The average increase in Mean Arterial Pressure was 13.80%. Blood pressure which differed significantly from the control Hean Arterial Pressure found at 1.3 and 5 minutes.

Ich (1970) observed the cardiovascular effects of Fancuronium browide, compaired with d-tubocurarine in patients undergoing cardiac surgery. The pulse rate showed a slight rise with both drugs, but these changes were not statistically significant. It will be seen that there was a significant fall in systolic, diostolic and mean arterial pressure by 5 minutes after the injection of d-tubocurarine and that these tended to return towards control values at 10 minutes with Fancuronium there was a significant rise in arterial blood pressure by 5 minutes after injection of the drug. 10 minutes after injection the mean values remained above control values but were not statistically different from control.

John et al. (1971) compare the chromatropic effects of gallamine in man with that of etropine, in addition to correlate heart rate changes with degree of neuromuscular block over a wide range of gallamine dosages. They observed that gallamine produced tachycardia that was greatest at a dosage of 100mg regardless of the method of administration. Heart rate increased further when atropine 2mg was given after gallamine, indicating that gallamine does not produce complete vagolysis. The magnitude of

tachycardia with gallamine was much less than that following atropine in either incremental doses of 0.2mg/kg. body weight or a sing& belus dose of 2.0mg/kg. body weight suggesting that gallamine may not act in the same manner as atropine.

Felman et al. (1971) investigated the effects of Pancuronium bromide (0.07mg/kg, body weight) on heart rate, mean arterial blood pressure, Cardiac out put and calculated total peripheral resistance in ten artificially ventilated patients anaesthetized with 60% NgO in exygen and phenoperidime (1mg/15kg body weight). According to their observation, Fancuronium caused a marked increase of heart rate (22-26%) and of mean arterial blood pressure (5-7%). These changes were all statistically significant.

gallamine (1 and 2mg/kg) produced sustained increases in heart rate for at least 20 minutes. The maximum increases were nearly same after 1 and 2mg/kg of gallamine, suggesting that the degree of tachycardia was independent of the dese used. This agrees with the study of Eisele et al (1971), who reported maximum tachycardia after 50-100mg of gallamine, mean arterial

Pancuronium causes slight rise in pulse rate or no change at all. Whereas with detubocuranine, there was decrease in pulse rate or no change. Rise in systolic blood pressure (36% of the cases) or no change was observed with Fancuronium, on the other hand fall in systolic blood pressure (56% of cases) or no change was observed with detubocuranine.

me fall of blood pressure with Paneuronium, on the other hand systolic blood pressure increased in all cases. There was a fall in systolic blood pressure of about 11.53mm of Hg (range 4-40mm of Hg) but the pulse rate was slightly increased, whereas with gallamine, there was increased in pulse rate and no change in blood pressure.

H

effects of Pancuronium bromide with detubocuranine chloride in anaesthetized patient was done by Mrs. Shargwa et al. (1978). They concluded that in 34% of patients there was no any change in pulse rate. The rise in pulse rate of about 0 to 10 per minute in 12% of the patients and 11 to 20 per minute in 4% of patients was observed. They were also observed that

in blood pressure ranging from 0 to 10mm Mg in 40% of patients, 11 to 20mm of Mg in 20% of patients, 21 to 30mm of Mg in 12% patients, 31 to 40mm of Mg in 4% of patients and 50 to 60mm of Mg in 4% of patients and 50 to 60mm of Mg in 4% of patients and 50 to 60mm of Mg in 4% of patients. Thus Fancuronium produced rise in blood pressure in 80% of patients. On the other hand the pulse rate and blood pressure both were decreased with d-tubocuronine.

Singh (1979) in 50 adult patients, repeated observations were made of sytolic blood pressure and pulse rate.

Maximum changes in blood pressure associated with Pancuronium were noted over the base line level i.e. before induction of ansesthesis. As all the cases were given halothane which has got the property of causing hypotension and bredycardis and this fact was kept in mind. In 48% cases there was slight rise of blood pressure while in 38% cases there was moderate rise in blood pressure. In 10% cases there was a severe rise in blood pressure which remained within normal limit.

Maximum changes in pulse rate associated with Pancuronium

were recorded. In 90% cases there was tachycardia. In 72% cases there was stight tachycardia while in 6% cases there was moderate tachycardia. In 10% of cases there was bradycardia but it was within normal limits.

and Pancuronium produced increase in heart rate in man principally by blocking vagal suscarinic receptors in the sinus node of the heart (Hughes et al. 1979). Both these drugs may also have indirect sympathomisatic effect. A rise in arterial pressure of 10-20mm Hg following the administration of Pancuronium and Gallamine is common (Stoelting R.K. 1973).

bromide on different clinical parameters in relation to gallamine triethedide and d-tubocuranue-hydrochloride. They observed that all the three muscle relaxants raised the pulse rate but, the increase in pulse rate was not significant with functionium and d-tubocurarine. There was however a significant rise in pulse rate with gallamine triethiodide. Fancuronium bromide and gallamine triethiodide caused minimal changes in blood pressure while d-tubocurarine caused hypotension in all most all the cases. The mechanism of action of

Pancuronium or Callamine on blood pressure is through the cardiac vagus in animal, in a manner similar to atropine. This is supposed to be the probable cause in man also, hypotension with tubocurarine in thought to be due to histamine refices and ganglionic blocking property, which is absent or minimal in Pancuronium.

Daksha et al. (1980) clinically compared Panguronius, with Tubocurarine and Gallamine. They were found that tubecurarine has a definite hypotensive effect. Callamine caused lesser fall in B.F. in some cases and a slight rise in others, while Pancuronium caused no fall in B.P. and in some cases there was a slight rise. Pulse rate was found to be reduced or consistent with tubocurarine, increase after Callamine and reised or consistent with Pancuronium. The same is confirmed by several published reports of workers in the past. Hypotension caused by tubocurarine is due to Ganglionic blockade and histamine release. Hypertension following Gallamine could be due to vagal blocking action causing tachycardia and also a direct stimulating effect on intracardiac beta receptores. Hypertension and tachycardia following Fancuronium is could be due to vagolytic and release of catecholamines.

Sheth et al. (1980) compare the cardiovascular effects of Pancuronium bromide with d-tubecurarine and Gallamine. They observed that there was no change in pulse rate in 60% patients with Pancuronium, 8% had a decline while 32% showed a rise. The meen rise was 3.62 beats per minute. The mean rise in pulse rate for d-tubecurarine and Gallamine was 1-20 best per mirate and 10-92 best per mirate respectively. There was no difference due to first or second dose. The rise in pulse rate with Pancuronium is a constant finding reported by many authors, Kemesaroff (1970) has noted that a rise in pulse rate was observed in case where the initial pulse rate was low but little change was observed in those cases whose initial pulse was high, a situation which is more likely to rise in emergency operations or condition like thyrotoxicesis and mitral stenesis where by any further rise in the already high pulse rate would be disastrous. There was no change observed in blood pressure in 40% of cases with Fancuronium, 4% had a decline while devation of blood pressure was observed in 56%. The mean rise was 5.40mm of Hg. With d-tubecurarine there was a mean fall of 9.60mm of Hg and with Gallamine a

mean rise of 6.76mm of Hg. There was no difference due to first or second dose. It has been observed that when  $N_2^{G=0}$  and fantanyl were used as maintance anaesthatic, the fall in blood pressure was significantly greater with d-tubocurarine than with Pancuronium, when halothane was substituted for femtanyl, detubocurarine produced a significant fall in blood pressure while Pancuronium did not produced a clinically significant change of blood pressure.

changes, Pancuronium increased heart rate, mean arterial blood pressure cardiac out put and pulmonary wedge pressure and it decreased systemic vascular resistance (P/O.O3). Although metocurine also increased heart rate and cardiac out put (P/O.O3) mean arterial blood pressure and pulmonary wedge pressure did not change d-tubocurine decreased all cardiovascular parameter except heart rate which increased significantly (Booi) et al. 1950).

him

According to Crul and Boolj 1980, no changes in arterial pressure and heart rate occured after giving Org NC 45 even in doses of up to three times the 95% blocking dose where as some degree of tachycardia and and increase in arterial pressure were usually seen

after giving Pancuronium.

Joshi et al. (1981) clinically compared Panguronium bromide. Callamine and d-tubocurarine in 150 cases. They observed that there was rise in blood pressure in 40% of patients with Pancuronium bromide. The rise in blood pressure ranging from O to 10mm of Hg in 32% of patients 10-20mm of Hg in 6% of patients and 20-30mm of Hg in 2% of patients. with Gallamine, rise in blood pressure was observed in 46% of patients. There was no changes in blood presure in 46% of patients with Passuronius and 36% of patients with Callemine. This rise in blood pressure caused by Pancuronius and Gallamine was not clinically significant. Rise in pulse rate was maximum (84%) with Gallamine. The range was 0-10 beats in 22%. 10-20% beates in 38%, 20-30 beats in 16% and 30-40 beats in 8%. With Panguronium, rise in pulse rate was observed in 64% of patients. The range was 0-10 beats in 40% patients, 10-20 in 16% of patients, 20-30 beats in 2% of patients. There was no change in pulse rate was observed in 28% of patients with Panouronium and 14% of patient with Callamine. This rise in pulse rats was not clinically significant. Comparing these regults. Fancuronium provided a better cardiovascular stability.

Administration of Org NC 45 minimal changes in the heart rate and blood pressure during the subsequent 40 minute in ratioms anaesthetized with Halothane or Englurane on the other hand, Fancuronium always increases the heart rate, Systolic and Diastolic blood pressure increased constantly but minimally after Pancuronium in patients anaesthitized with Halothane, whereas they did not change in patients anaesthetized with enflurane.

Sergio et al. (1982).

A comparative study of Org NC 45 and Pancuronium on heart rate and arterial pressure in ansesthetized man was done by Barnes et al. (1982). They observed that the effect of bolus dose of Org NC 45 on heart rate in lightly ansesthetized man is different from that Pancuronium. The dose of Org NC 45 used in this trial appears to be devoid of the vagal blocking action observed with Fancuronium. Animal studies which have shown Org NC 45 to be devoid of vagal blocking activity (Booij et al 1980, Durant, Houwerttes and Crul 1980) have confermed in man. The changes observed with Fancuronium are consistent with previously reported work (Kelsan and Fennedy 1971, Miller, Eger and Stevens 1975) when Fancuronium is used in clinical practice, a stimulus that produces a sympathetic discharge result

in tachycardia that would be more marked in the presence of vagal blockeds. Excessive tachycardia may occure when Pencuronium is used this would be less likely to occur with, Org NC 45. The effect of Pancuronium and Org NC 45 on mean arterial pressure to be dependent on the conditions prevailing at the time the deta were collected, Org NC 45 did not have a consistant effect on mean arterial pressure after a belus injection in the lightly anaesthetic used unstimulated subject, and changes that did occur were minimal. The injection of Pancuronium resulted in a small but significant increase in arterial pressure. This increase in mean arterial pressure did not appear to correlate with the increase in heart rate. The increase in mean arterial pressure during intubation after Org NC 45 was modest and consistant. The increase in mean arterial pressure in those patient who had received Pancuronium was greater and tended to inconsistant.

In clinical studies on Org NC 45 comparison with Pancuronium, by Karr et al. (1982). The heart rate and arterial systolic pressure changes for the first 50 minutes following injection of the intubating

does of each drug. At 15 minutes following injection of Org NC 45 and when the surgical stimulus was absent or minimal there was no evidence of tachycardia, this agrees with the findings from other clinical studies of this drug. Animal experiments have shown that in contrast for Pancuronium and other nondepolarizing muscle relaments Org NC 45 in doses 20 times greater than those required for neuromuscular blockade, has no effect on the heart rate, arterial pressure or the sympathatic nervous system (Marshall et al. 1980).

Cardiovascular effects of Org MC 45 and Panguronium were examined in seven anaesthetized dogs by 5. Titzal et al. in 1983, They found that equipotent doses of Org NC 45 (0.025mg/kg) and Paneuronium (0.03mg/kg). Heart rate increased significantly from 104.5±9.9 to 121.1+8.6 best per minute after Pancuronium (P/0.05) whereas Crg NC 45 has no effect. Neither drug had any effect on systolic disstolic or seen arterial pressure. Tachycardia observed in their study after I.V. administration of Fancuronium was dose related. No increase in heart rate was found by Miller and colleogues (1975) nor was it reported in the experimental study Demenoch and colleagues (1976), it was however describe in a clinical investigation by Parmenteir and Dagnetic (1979). Org NC 45 irrespective of dose and type of application did not induce any changes in heart rate or systemic

pressure. Thus Org MC 45 administered in clinical doses does not induce any vagalytic activity. Moreover, there was no evidence of direct instropic action on myocardium.

Enghack et al. (1983) observed the cardiac effects of Vecuronium and Pencuronium during Halothane anaesthesia in 20 adult female patients scheduled for gynaecological operation. According to their observations, Pancuronium 0.08mg/kg caused increased of 20% heart rate after 1 minute. Heart rate remained unchained for the following 10 minutes and was significantly greater during the first 5 minute compared with the group receiving Vecuronium. An increase in mean arterial pressure of 8% was seen one minute after the injection of Fancuronium, Vecuronium 0.057mg/kg caused no changes in heart rate and no significant changes in mean arterial pressure.

The cardiovascular effects of Veguronium bromide and Fancurenium bromide were compared by Shatia and Mrs. Dave (1985) in 50 patients between the age of 40 to 60 years scheduled at for elective major cancer surgery. They observed pulse rate for first five minutes and then up to 15 minutes, shows

that there is no change in 60% to 72% of cases with Vecurenium while with Pencuronium there is definite tachycardia in all patients. Robert B. Morries et al. (1983) observed the same effects, may stated that tachycardia produced with Pancuronius are due to its vagolytic and sympathonimatic properties. While Org NC 45 being devoid of autonomic neural activities. It does not produced any cardiovascular effects (Gregoretti et al. 1982). Gallamine causes atropine like response and produces tachycardia and Pancuronium produces similar effects although responses is less profound. They also noticed changes in arterial systolic blood pressure during first five minutes and up to 15 minutes. The observation shows that with Vecuronium there was no change in B. . in 44% to 68% of cases while with Pancuronium 96% to 98% of cases there was increase in Blood Pressure, Moris et al. observed that pulse rate and mean arterial blood pressure did not changes following Vecuronium, while increased 22% and 24% respectively following Fancuronium.

The effect of Atracurium, Vecuronium and Pancuronium on heart rate and arterial blood pressure in normal individuals were studied by Lavery et al. (1986). Heart rate and rhythem (from ECG) and systolic,

diastolic, and mean arterial pressure (using an caseillotonometer) were measured for 30 minutes following administration of atracurium 0.5mg kg 1, Vecurenium Smg kg or Pancuronium O. tag kg during steady - state anaesthesia, with nitrous oxide, oxygen and either 0.75% halothane or fentanyl 4-5 ug kg 1. With halothane anaesthesia Atracurium causes only minimal changes in Heart rate, Systolic arterial pressure, Mean arterial pressure, Diastolic arterial pressure, although these were statistically significant at times. The Heart rate changes after Vecuronius were minimal (a maximal fall of 75PM or about 9%). Changes were significent (P/0.05) at 1 and 30 minutes. There was significant fall (P/0.05) in Systolic erterial pressure and Mean arterial pressure (up to 15 and 19% respectively) during the period 3-15 minutes after administration of Vecuronium. Diastolic erterial pressure showed a significant decrease (F/0.05) throughout the 30 minute period. Heart rate after administration of Pancuronium was significantly increase (F/0.01) within 1 minute and remained as (F/0.001) at every subsequent observation. There were no significant changes in Systolic or Diastolic arterial pressure but Mean arterial pressure rose significantly (P/0.01) in the 3 minutes after administration of Pancuronium

with fentanyl ansesthesis. Atracurium produced gradual reduction in Heart rate, becoming significant (P/0.05) of the 20,25, and 30 minutes observations when the decrease was of the order of 5-6%. Three to five minutes after administration of Atracurium, Systolic arterial pressure, Diastolic pressure and Mean arterial pressure were decreased significantly ( [ 10.05) but from that point erterial pressure began to increases and by 25-30 mimstes was significantly greater (P/0.05) than the control. The Vecuronium showed no significant changes in Heart rate. Arterial pressure showed significant reduction (PZO.05) 3-5 minutes after Vecuronium administration. However by 30 mimutes, Diastolic arterial was significantly greater (F\_0.05) than the control. Heart rate after Paneuronius had significantly increased (P/0.01) at 1 minute and remained as (P/O.001) up to and including, the 30 minutes observation. Systolic arterial pressure significantly increased at 5.15, 20 and 30 minutes. Diastolic arterial pressure and Mean arterial pressure were increased from 1 to 30 minutes after Fancuronium administration.

Singh et al. (1987) observed the comparative effects of Pancuronium and d-tubocurarine in major abdominal surgery. They concluded that Pancuronium

produced a rise in systolic pressure in 30% cases while in 12% cases there was no change. Tachycardia was observed in 4% cases, the other 16% cases had no change in heart rate.

According to Mrs. Jana et al. (1988) Vecuronium did not produced any clinically important effect on the pulse rate and systolic blood pressure although intubation after Vecuronium did cause a significant rise in pulse rate any systolic blood pressure. These cardiovascular effects were similar to those reported by Morries et al. (1983).

the Vecuronium with Pancuronium and observed that mean pulse rate and mean arterial blood pressure were elevated to a highly significant level during intubation which satteled after about 10 minutes to a level above the preinduction level with both drugs, but rise in pulse rate and mean arterial blood pressure was significantly less (P/.001) with Vecuronium as compared to pancuronium both during intubation and after 10 minutes of injection of muscle relevants. This is in conformity with the views of Barner et al. (1982). Mild tachycardia and slight rise in Mean arterial pressure after 10 minutes of injection of Vecuronium

may be because of light plane of anaesthesia in this study since no other norcotic or inhalatinal agent other than N2O was used. So they concluded that Vecuronium bromide had better cardiovascular stability as compared to Pancuronium.

and Pancurium were compared (Singh et al. 1990). They found that patients receiving Pencuronium showed significantly higher mean pulse rates 5 and 10 minutes after this relaxant. The second dose of Pancuronium also resulted in significantly higher pulse rate 5 minutes after it. The mean arterial blood pressure 10 minutes after the initial dose of Pancuronium was significantly higher than the corresponding mean value of atracurium. The mean arterial pressure after the second doses of the two relaxant were comparable.

heijel et al. (1990) clinically compaired
the Fancuronium, Vecuronium and Atracurium. They
observed that a significant increases in pulse rate
was seen in patients receiving Fancuronium, With
Vecuronium there was an initial rise fellowed by fall
in pulse rate. In patients who received atracurium
showed a slight fall in pulse rate. Patients receiving

Pancuronium showed a significant increase in mean arterial pressure while patients receiving Vecuronium or Atracurium exhibited a stable blood pressure without much rise or fall even after intubation.

Muralidhar et al. (1990) compare the Vecurenium and Paneuronium during surgical treatment of patant ductus arteriosus. They observed that the heart rate in patients receiving Pancuronium were significantly increases (F\_0.05) from 119.1-12.4 and 122.7-9.9 after the administration of the relament and after endetrachial intubation respectively. In patients receiving Vecurenium there was no significant changes in the heart rate at these events. The systolic blood pressure with Paneuronium rose significantly from a preinduction value of 116.0±16.2mm Hg to 130.7±12.4mm Hg and 130.0±11.4mm Hg after the administration of the relaxant and after endotrachial intubation respectively. The systolic blood pressure with Vecuronium fall alightly but significantly from a preinduction value of 121,0±15.1mm Hg to 114.7:10.1mm of Hg after the administration of relaxant but rose back to the control value after the endotrachial intubation. There was no significant change in diastolic blood pressure after relaxant administration and endotrachial intubation in patients receiving Vecurenium, Whereas there was a significant

increases in the diastolic blood pressure in patients receiving Pancuronius when the preinduction value was compared to the post relaxant and post intubation values.

singh et al. (1990) compared the cardiovascular effect of Atracurium and Pancuronium. They observed that Pancuronium showed significant higher pulse rates 5 and 10 minutes after this relament. The second dose of Pancuronium also resulted in significantly higher mean pulse rate 5 minutes after it. The mean arterial pressure 10 minutes after the initial dose of Fancuronium was significantly higher than the corresponding mean value with Atracurium.

#### CALLANDES TRESTRUODIDE

In 1947, Bovet and his cowerkers describe a synthetic muscle relaxant gallamine triethicdide. The effects of this relaxant in man were first described by Huguendard and Boue (1948) in France and by Mushin and his colleagues (1949) in England.

Gallamine triethiodide in chemically tri (D-diethylaminoethoxy) - Benzine trithiodide, It is white amorphous powder, nonirritant, relatively stable and available in 40mg/ml solution in 2ml and 10ml ampules.

$$0-CH_{2}-CH_{2}-N^{+}-(C_{2}H_{5})_{3}$$

$$0-CH_{2}-CH_{2}-N^{+}-(C_{2}H_{5})_{3}$$

$$0-CH_{1}-CH_{2}-N^{+}-(C_{2}H_{5})_{3}$$

### STRUCTURAL FORMULA OF CALLANGE TRIENTIONICS

The intravenous bolus of Gallamine triethiodide (1.5-2mg/kg) is the most preferred rout with the average dose of 100-140mg for total cossation of respiration and muscular relaxation. The onset of action occurs within 90-120 second and duration of action between 20-30 minutes, when injected subcutaneously the activity is about one

quarter that of an intravenous injection. It is inactive by months. Supplementary doses of gallamine 20-40mg are given as required.

Junction by mondepolarization block. The curare molecule combines with the end plat. receptors and this denies the acetylcholine molecule access to its normal destination.

about 30-100 percent is excreted unchanged in urine within two houres (Mushin et al. 1949). Prolonged paresis may follow the use of gallamine in cases with poor renal function. (Fairley 1950, Montgomery and Bennett-Jenes 1956, Faldman and Levi 1963). This is partly due to less of redistribution sites in the kidney and also due to the lack of alternative path ways of excretion for the drug (Feldman et al. 1969). It is bound to serum albumin and the increase in potency by increasing the pN. Senstivity occurs in myesthenia grevis and in the presence of anaesthetics with a curare like action such as ether.

Gallamine produced tachycardia in man by blocking the vagal muscarinic receptores in the sinus

mode of the heart Brown et al. 1970 and by indirect sympathemimalic effects. The tachycardia in man is dose dependent to gallamine, reaching a maximum at img/kg. 100% heart rate may increases if the patients base line rate was alow, Gallamine is strongly vagolytic in the neuromuscular blocking dose range, often resulting in heart rate of 90 to 120 beats per minute in the presence of adequate neuromuscular blockade.

A rise in arteriol pressure of 10 to 20mm Hg following the administration of Gallsmine is common (Stoelting 1973) in the absence of potent anaesthetic. Increased heart rate secondary to the vagelytic effect of this drug in the absence of any fall in peripheral resistance is the probable mechanism involved.

Gallamine have been produce weak positive instropic effects in cardiac muscle (Brown et al. 1970). Release of catechelamine may be increased within the heart or relative shift of autonomic tene to the edrenmergic side in the beart due to cardiac muscarinic receptor block.

In normal san Gallamine increase cardisc out put without any important change in peripheral resistance.

Cardiac out put increases in the range of 25 to 53% after 0.5 to 2.0mg per kilogram given as a belus intravenously and sustained for 5 to 20 minutes.

Arrhythmics after administration of gallamine may occur as a result of:

- (1) Suddan shift of autonomic balance toward the adrenergic side due to the vagal-blocking effect the drug (Frown et al.1970).
- (2) A possible sympathomizatic effect.
- (3) A relatively great inhibition of the aterioventricular node than the simus node. These mechanisms may be manifest clinically as single or multifocal premature vestricular contractions or ventricular tachycardia or nodal tachycardia under light helothane or cyclopropane anaesthesis. In known simus nodal disease, a vagolytic effect might cause a relatively greater increase in the spontanious rate of activity of the atrioventricular node than the simus node, result is nodal tachycardia.

callamine inhibit muscarinic receptores this action is an atropine like effect and is limited to cardiac receptores. There is no effect on bowel, salivary glands, pupil or other muscarinically inervated end organs. Experimentally, both vagal induced bradicardia and bradicardia secondary to acetylcholine or methacholine are blocked (Hughes et al. 1976).

There is no evidence available to suggest that gallamine has any action on the central nervous system in man. It has no any direct action on liver and kidney. Indirectally, however, it has a weak inhibitory effect on the plasma cholenesterase produced by the liver.

#### FANCURON UM BROWTOR

Pancuronium bromide was introduced in clinical anaesthesia by Baired and Reid in 1967. It is a odurless, while crystaline powder with a bitter test, it melts at 215°C with decomposition.

Chemically Pencurenius bromide is a bis-quaternary assonius compound which is relatively stable and is supplied for clinical purposes in 2ml ampules containing 2mg/ml.

The intravenous bolus of Pancuronium (0.08 to 0.1mg) is the most preferred route with the average intubation dose 5 to 8mg, onset of paralysis occur within 1.5 to 3 minutes. The paresis produced by Pancuronium last for about 25 to 45 minutes and a satisfactory "topping up dose" is about 1/5 to 1/10 of the original paralysing dose.

Pancuronium acts at the neuromuscular junction in man by non-depolarisation (Baird and Reid 1967).

mainly unchanged in the urine, but can be birdegraded to less active and inactive compound by metabelism of the 3 and 17 acetyl groups of the parent compound. Up to 15% of an injected dose of Pancuronium may be recovered from urine as 5-hydroxy derivative. In the absence of remal excretion large amount of the drug can be recoved from the bile much in the form of steroids in which the or 17 acetyl group has been hydrolysed to either the hydrogen or hydroxy derivative.

Like all the muscle relaxants it is a highly charged ion and is therefore unlikely to pass vital membranes easily. There is no evidence available in man that it is not believed to cross blood brain barrier.

It possesses very little fat solubility.

Pancuronium has little effect on the cardiovascular system Baird and Reid 1967, Levin et al. 1971). There is little changes in pulse rate in doses less than C.Obmg/kg although some vagolytic activity occures at higher dose levels. It has been suggested that Pancuronium may tend to produced an increase in blood pressure by sympathetic stimulation, especially in the presence of autonomic irritability. Evidence suggested that Pancuronium produced a direct but short lived instrupic effect upon the intact heart. It increases the peripheral resistance. Because of the absence of hypotension this drug is preferred for patients with cardiovascular instability and in low out put states.

There was no evidence suggested histamine release after administration of Fanouronium. This is believed to account for the absence of both hypotension and bronchospass following its use: however allergic reactions have been reported (M.C-dowell and Clark 1969, Nama et al. 1972).

Pancuronium can be easily reversed by neostigmine in the usual manner. Pancuronium is a weak inhibitor of

plasma cholinesterase, but some of its metabolic derivatives are more active in this respect.

### VECURORIUM BRONIDE

Vecuronium bromide was originally known by its research code CRC NC 45 and was developed by Dr. David Savage of organon Technika laboratories (Savage et al. 1980). Vecuronium was developed by non hormonal properties of steroid molecule, which is an androstanyl derivative of acetylcholine.

vecuronium bromide is a buffered freeze-dried powder, available as was per ampoule, with iml ampoule of water for injection as solvent. The ampoule of powder can be kept for 3 years provided they are stored in the dark at a temperature below 25°C.

The trade name of Vecuronium, Morcuron, reflects the fact that 'nor' indicates, that Vecuronium has exactly the same chemical structure as Fancuronium except for the absence of a methyle group. The missing methyle group is the one which is attached to the quaternary mitrogen atom which is itself attached to the A ring of the steroid neucleus, Vecuronium is

a Monoquaternary hosologue of Fancurenium, having negligible ganglion blocking and vagolytic properties (Agoston et al. 1980).

### CHEMICAL FORMULA OF VEGUPORIUM

Vecuronium in the dose of 0.1mg/kg have been reported to produce excellent to good intubating condition in 90 seconds (Mirbhur et al. 1983). Large doses of Vecuronium (0.15 to 0.2mg/kg) improve intubating condition at 1 minute after their administration, such

that at least 60% of patient can be regarded as excellent and after 90 seconds produces such condition in 90-95% subjects and at this time there is no difference whether 0.1mg/kg of Vecuronium or twice of this amount has been given. Intubation is unlikely to be smooth or may not even succeed with doses below 0.25mg of Vecuronium despite waiting for adequate time after administration.

The maintanance dose of Vecuronium is 0.03 to 0.05mg/kg body weight. The duration of effect is 10-20 minutes. However the larger doses of Vecuronium could lead to a prolonged total duration of action. It is metabolise in the liver and mainly excreted in the bile, a small quantity is also excreted in the urine.

than adologats. The duration of effect after 0.07mg/kg was 73 minutes thus Vecuronium has a larger volume of distribution in infants and children than in edologats and adults.

The neuromagular effects of Vecurenium are petentiated by both respiratory and metabolic acedesis. The alkaline medium accelerates the decomposition of Vecuronium. The petentiating effects of hyperventilation on the duration of neuromagular block are probably minimal in clinical practice.

Clinical degree of hypercapnia or hypokapnia established after but not before the administration of Vecuronium are associated with changes in twitch tension compared with normocapnic condition. An increase in arterial PCo<sub>2</sub> is associated with a decrease in twich tension and vice versa.

The cumulative effects was not seen after repeated doses of Vecuronium.

On heart rate and arterial pressure (Febey et al. 1981, Savage et al. 1980) and their lack of sympathetic stimulation and vagal-blocking effect make them superior to gallamine, Pancuronium and fazadinium (Engheek et al. 1983). In vitro tissue preparation show that Vecuronium possesses an antimuscarinic action 1-3 times less than Pancuronium.

Spontaneous recovery of neurosuscular function without necessarily involving the need for a specific antidote. Antagonism of the neurosuscular block produced by Yeouronium can be achieved with antichelimenterases such as neestigaine in the dose of 0.04 to Obag/kg body weight with 1.2mg of atropine (Marshall et al. 1980).

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MATERIAL AND METHOD

The present study was conducted in the department of Ansesthesiology in N.L.B. Nedical College and Rospital Jhansi (U.R.) during year 1990-1991, with the six to compare and evaluate the effects of Vecuronium, Pancuronium and Callasine over the cardiovascular system.

Ninty adult, indoor patients of either sex between 20 to 65 years of age scheduled for various elective surgical procedures, requiring trachial intubation and muscular relaxation under general anaesthesia, comparized the material for study. Fatients were divided in to three groups of 30 each. Each group was given one particular relaxant during anaesthesia, intients having any henal, Hepatic or Cardiovascular disease were excluded from the study.

All the patients were physical status as A.S.A. grade I or II. They were throughly examined preoperatively to the clinical fitness. Routine investigations along with relevant special investigation were performed in all the patients, only patients with normal investigations were accepted for the purpose of study. An informed written

consent was obtained from every selected patient, and they were kept empty stomach for at least 6 hours before the induction of anaesthesia.

Premedication consist of injection atropine

O.6mg and injection dissepan 10mg both intramuscularly,

30-45 minutes prior to the induction of annesthesis.

Venepuncture was performed with a 16 or 18 gauge I.V. Cannula under proper aseptic condition.

A 5% Dextrose in D/V was started, pulse, systolic and diastolic blood pressure were recorded two minute prior the induction of anaesthesis to serve as a base line records.

Pre-exygenation with 100% oxygen was initiated 5-5 minutes prior to the induction. Induction of ansesthesia was performed with the sleeping dose (4 to 6mg per kg body weight) of 2.5% Thispantone Sodium slowely, till abelition of eye lash reflex. Intubation was done by proper size cuffed endotrachial tube with Suxamethonium in the dose of 1.5 to 2mg per kg body weight (80-100mg), connection were made to attach the patient with the Napleson A circute of Soyel's Apparatus, 1.P.P.V. was continued.

when the effect of suxamethonium completely were out the chosen nondepolarizing muscle relaxant administered in the following manner.

### GROUE-X (Vecuronium group) 30 patients

All these patients received Vecuronius in the doses of O.OGmg per kg body weight intravenously.

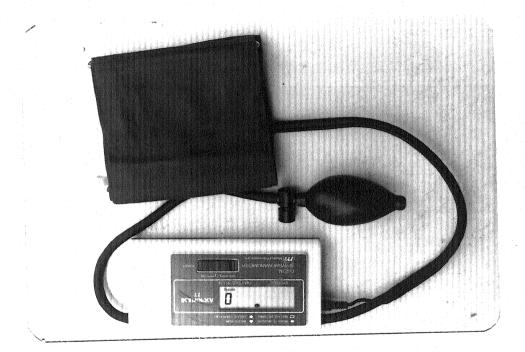
## CHCUP-II (Pancuronium Bromide) 50 patients

All these patients received Pancuronium in the doses of O. Tag per kg body weight intravenously.

# ORCU:-TII (Gallamine Friethiodide) 30 patients

All these patients received gallamine in the doses of 2mg per kg body weight intravenously.

and exygen (65:35) I.F.F.V. was carried out but hyperor hypoventitation was avoided. Supplemental dones of
Pethidine were given to maintain analysis during
surgery. No other volatile inhelational anaesthetic
was used during the procedure. Incremental desage of
muscle relaxants were given in the dose Vecuronium
O.O2mg per kg body weight, Pancuronium O.O2mg per kg
body weight, as and when required.



ASTROPULSE 77 (digital aphysmomenometer)

Pulse, systolic blood pressure and disstolic blood pressure were recorded. Pulse and blood pressure were recorded with Astropulse 77 (digital sphygmomanometer) every 5 minutes after giving the muscle relaxants.

movements in the rebreathing bag the residual relaxants were antagonised with 1.2mg Atropine and 2.5mg Neostigmine intravenously. Patients were extubated after establishment of spontaneous respiration. Suction was done for clearing the oral cavity from secretion just before extubation and after extubation. Patients were oxygenated with 100 percent oxygen for 5 to 10 minutes after extubation. Post operative pulse rate and blood pressure were recorded.

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CBSERVATION

In the present study the effects of Vecuronium, Pancurenium and Gallamine were compared and evaluated on cardiovascular system in 90 patients. The patients were of both sexes and over the age of 26 years but below the age of 65 years.

These minety patients were randomly alocated in to three groups depending upon the type of muscle relaxant used. Each group was comparised of 30 patients.

### AGE AND SEX DISTRIBUTION

Out of thirty patients in group I, 3 patients were between the age group of 20-30 years, 10 patients in 30-40 years, 5 patients in 50-60 years and 4 patients were in the 60-70 years of age (Table I).

In group II 3 patients in the range of 20-30 years, 9 patients in the range of 30-40 years, 9 patients were in the age group of 40-50 years, 4 patients were 50-60 years and 5 patients were between the 60-70 years of age (Table-I).

PARLE \_ I SHOWING THE AGE DISTRUBUTION OF THE PARLETTS

|        |    |     | and the second s | and the second second |             |          |  |
|--------|----|-----|--|-----------------------|-------------|----------|--|
| Age in |    |     |  |                       | Grown I     |          |  |
| yeers  |    |     | Part of the said   |                       | Calibrating |          |  |
|        |    | * % | no.oz<br>Patienta  | *                     | Potienta    | <b>%</b> |  |
| 20-30  | 3  | 10  | 3  | 10                    | 2           | 7        |  |
| 30-40  | 10 | 33  | 9  | 30                    | <b>5</b>    | 17       |  |
| 40-50  | 8  | 27  | 9  | 30                    |             | 40       |  |
| 50-60  | 5  | 17  | 4  | 13                    | 7           | 2.3      |  |
| 60-70  | 4  | 13  | 3  | 17                    |             | 13       |  |
| lotal. | 30 | 100 | 30   | 100                   | 30          | 100      |  |

In group III out of 30 patients 2 patients were between the age group of 20-30 years, 5 patients were 30-40 years, 12 patients were 40-50 years, 7 patients were 50-60 years and 4 patients were in age group of 60-70 years (Table I).

SHOWING SEX DISTRIBUTION OF THE PATTENTS

|        | <u> </u>          | Cross-LL<br>Passuronius | Gram III<br>Gallamine |     |
|--------|-------------------|-------------------------|-----------------------|-----|
|        | No.01<br>Patients | Wo.of<br>Patients %     | No.01<br>Potients     |     |
| Nale   | 18 60             | 16 53                   | 11 37                 |     |
| Female | 12 40             | 14 47                   | 19 63                 | di. |
| Total  | 30 100            | 30 100                  | 30 109                | ja. |

In the present study 45 patients were male while remaining 45 were female. In group I the male female ratio was 18:12. In group II and III this ratio was 16:14 and 11:19 respectively (Table II).

SHOWING THE WEIGHT DISTRIBUTION OF THE PARTER'S

| Volght | <u>Great</u><br>Vegure | Green_1<br>Vecuronium |   | Gram_II<br>Pencuronium |                   | Grown IXI<br>Gallamine |  |
|--------|------------------------|-----------------------|---|------------------------|-------------------|------------------------|--|
| 1.n    | AG.O:<br>Fatients      | ).                    | No.e.<br>Patients                       |                        | No.or<br>Fatients | 56                     |  |
| 40=50  | 6                      | 20                    | *************************************** | 17                     | 9                 | 30                     |  |
| 50-60  | 15                     | 50                    | 15                                      | 50                     | 16                | 53                     |  |
| 60-70  | 6                      | 20                    | 7                                       | 23                     | 3                 | 10                     |  |
| 70-80  | 3                      | 10                    | 3                                       | 10                     | 2                 | 7                      |  |
| Total  | 30                     | 100                   | 30                                      | 100                    | 30                | 100                    |  |

patients (20%) were in weight group of 40-50 kg, 15 patients (50%) in 50-60 kg., 6 patients (20%) in 60-70 kg. and 3 patients (10%) in the 70-80 kg of weight group (Table III).

In group II 5 patients (17%) were between 40-50 kg. of weight 15 patients (50%) were between 50-60 kg., 7 patients (23%) were between 60-70 kg and 3 patients (10%) were between the 70-80 kg of body weight (Table III).

Out of 30 patients in group III 9 patient (30%) were in the weight group of 40-50 kg., 16 patients (53%) in the 50-60 kg., 3 patients (10%) in the 60-70 kg and 2 patients (7%) in the weight group of 70-80 kg. (Table III).

SHOWING THE VARIOUS TYPE OF SURGICAL PROCESURES

| Surgical<br>Procedures                  | Graup_I<br>Vecuronium | STMP_IL Pancuronium | Gallemine  |  |  |
|---|-----------------------|---------------------|--|--|--|
| Cheledochelith<br>and<br>Chelecystectom |                       |                     | auranian kan saar akka dari aka dari aka dari aka saar sa territar saar akka akka akka akka akka akka ak |  |  |
| Appendicectomy                          | 6                     | 4,                  | 3  |  |  |
| Herniorrhaphy<br>and<br>Herniotomy      | 4,                    | 2                   | 3  |  |  |
| Cophoractomy                            | 6                     | 3                   | 5  |  |  |
| Abdominal<br>Hystrectomy                | 3                     | 8                   | 14   |  |  |
| Thyroidectomy                           |                       | 3                   | 4000   |  |  |
| Elective<br>Caesarean<br>Section        | 44                    | 2                   | 1  |  |  |
| Urological                              | 4                     | 3                   |  |  |  |
|   | 30                    | 30                  | 30   |  |  |

Table IV shows the types of operation in which the drugs were used. In Vecuronium group Appendicectomy were performed in 6 patients, Hernierrhaphy and Hernietomy in

A patients, Copharectomy in 6 patients, Abdominal Hystrectomy in 3 patients Thyroidectomy in 3 patients, Elective Caesarann section in 4 patients and Urological operation were in 4 patients (Table IV).

In group II Pangurenium was used to facilitate

for Cholocystectomy and Cholodocholithotomy in 5 patients.

Appendicectomy in 4 patients, Hermiorrhaphy and Hermiotomy

in 2 patients, Copherectomy in 3 patients, Abdominal

Hystrectomy in 8 patients, Thyroidectomy in 3 patients,

Elective Caesarean Section in 2 patients and Urological

operation in 4 patients (Table IV).

In group III muscle relaxation was provided with Gallamine for Cholocystectomy in 4 patients, Appendicectomy in 3 patients, Herniorrhaphy and Herniotomy in 3 patients, Cophoractomy in 5 patients, Abdominal Hystrectomy in 14 patients and Elective Caesarean Section in 1 patient (Table IV).

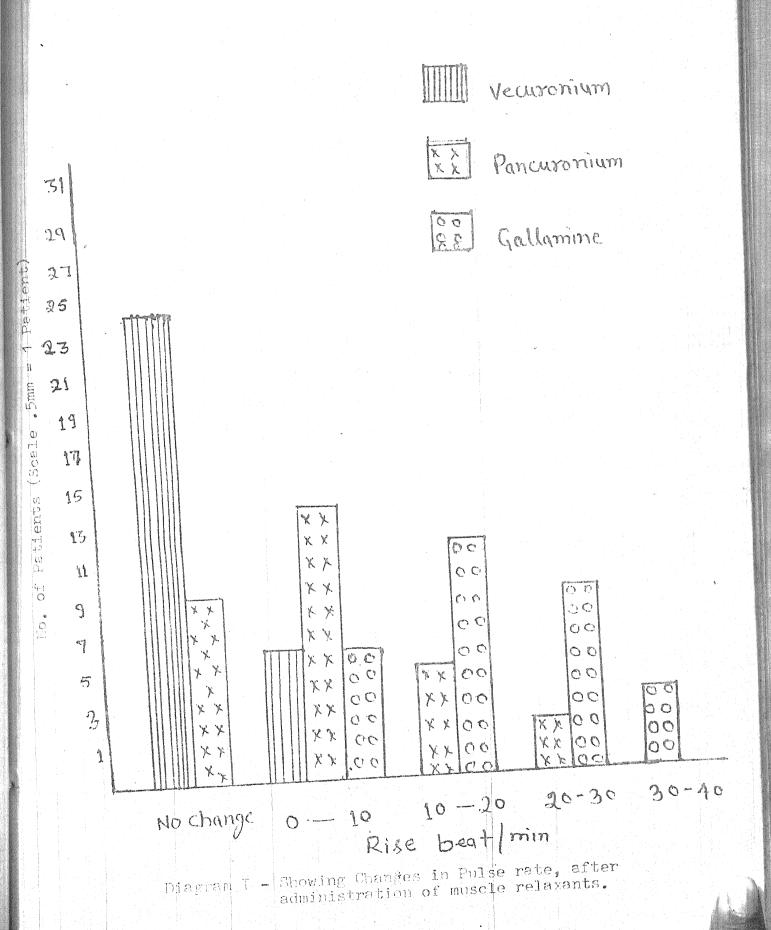
SPORTED CHANGE IN PULSE DATE FOLLOWING THE ANNIHUSTRATION OF AUGUST BEST AND AUGUST AND THE ANNIHUSTRATION

|                         |                      |     |                    | Market and and any or any  | 1480 State Control of  | Secretarion Control |
|-------------------------|----------------------|-----|--------------------|--|--|---------------------|
| Change in               | Greureni<br>Vecureni |     | Pancuron           | none.  | Graun<br>Gallem  |                     |
| Pulse Rate<br>Beat/Min. | No.o.<br>Patients    |     | lo. ol<br>Patients | <b>%</b>   | Mo. of<br>Patient  |                     |
|                         |                      |     |                    | Girli Maria Ma | Section of the confidence of t |                     |
| No change               | 24                   | 80  | 9                  | 30   | ***  | 460                 |
| Rise 0-10               | 6                    | 20  | 14                 | 46   | 6  | 20                  |
| Rise 10-20              |                      | 480 | 3                  | 17   | 12   | 40                  |
| Rise 20-30              | 4846                 | 484 | 2                  | 7  | 9  | 30                  |
| Nise 30-40              | ###                  |     | ***                | 480  | 3  | 10                  |
|                         |                      |     |                    | Andrew March   |  | at the first        |
| Total.                  | 30                   | 100 | 30                 | 100  |  | 100                 |

### PULSE RATA

In Vecurenius group there was no change observed in 80% of patients while in slightly rises (0-10 bests/min.) was recorded in 20% of patients (Table V).

of patients in Fancurenium group. 70% of patients in this group showed rises in pulse rate. The range was 0-10 beats in 46 percent, 10-20 beats in 17 percent, and 20-30 beats in 7 percent of patients (Table V).



Fatients received Gallemine showed marked rise in pulse rate. The rise in pulse rate ranging from 0-10 beats in 20% of patients, 10-20 beats in 40 percent, 20-30 beats in 30 percent and 30-40 beats per minute in 10 percent of the patients (Table V).

TABLE - V.
SHOWING CHANGE IN BLOOD PRESSURE NARGE FOLLOWING THE
MISTOR GRANGE VERY CONTROL OF THE

| Change in               | Systelie Blee  | d Processo | Diagtolic Blood | Pressure |
|-------------------------|----------------|------------|-----------------|----------|
| Blood Pressure<br>an Hg | No. of Patient | 3          | No.ef Patients  |          |
| No change               |                | 83         | 26              | 87       |
| Rise 0-10               | <b>9</b>       | 17         | 4               | 13       |
| Rise 10-20              |                | 480        |                 | ***      |
| Rise 20-30              | 樹藤             | 1899       | ***             | •        |
| Rise 30-40              | disk           | 4880       |                 | ***      |

#### BUOOD PRESQUES

pressure was observed in 83% and 87% of patients respectively in Vecuronium group. Slightly rise in blood pressure was recorded in 17% of the patients. The rise in systolic blood pressure in the range of 0-10 mm Hg in 17% of patient while 15% patients showed rise in disatolic blood pressure in this range (Table VI).

X X Systolic Blood Pressure

t t Diastolic Blood Pressure

| 2.1   |  |       |  |
|---|--|-------|--|
|   |  |       |  |
|   |  |       |  |
| 27  | Agrana and an annual agrant and agrant agran |       |  |
| , and the same of |  |       |  |
| to act  | r-1++  |       |  |
| 35  | XXX  |       |  |
| 477   | 17/4   |       |  |
| 8 23  | 1. 4 1   |       |  |
| La La Carta   | XX   |       |  |
| ç   | ++   |       |  |
| 21  |  |       |  |
| 15 35 17 25 17 21 21 21 21 21 21 21 21 21 21 21 21 21   | XX   |       |  |
|   | 1 1+1  |       |  |
| 11  |  |       |  |
|   | XX X   |       |  |
| 0 17  | + +  |       |  |
|   |  |       |  |
| 8 15  | 1XX  |       |  |
| 5 17  | 1 1 + 1  |       |  |
|   |  |       |  |
| 13  | 1xx  |       |  |
| 9   | 1++  |       |  |
|   | 1++  |       |  |
| 11  | XX   |       |  |
| ω<br>α.   | 1 + +  |       |  |
| 4   |  |       |  |
| No. of Petients (Seale  | 1xx  |       |  |
|   | + +  |       |  |
| £ 7   |  |       |  |
|   | Y X  |       |  |
| 5   | * * *  | XX    |  |
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| 3   |  | XX    |  |
| J.  | The state of the s | 4 4-1 |  |
|   |  | XX    | and a contract of the contract |
| 1   | 1.4. +   |       | A CAMPA THE RESIDENCE OF THE PROPERTY OF THE P |
|   |  |       |  |
|   |  |       |  |

No change 0- 10
RISC mining

Diagram II - Showing change in Blood Pressure
after administration of Vecuronium

SHOWING BLOOD PRESSURE RANGE FOLLOWING THE ADMINISTRATION OF ZANGURARIUM

| Change in      | Systolic Blood  |     |              | ood Pressure |
|----------------|-----------------|-----|--------------|--------------|
| slood Pre-     | No. of Patients |     | No.of Patien | da %         |
| asure<br>am Hg |                 |     |              |              |
| No change      | 12              | 40  | 12           | 40           |
| Rise 0-10      |                 | 27  |              | 30           |
| Rise 10-20     | 6               | 20  | 7            | 23           |
| Rise 20-30     | 4               | 13  |              | 7            |
| Rise 30-40     | 400h            | 460 | <b>1990</b>  | <b>1889</b>  |
| Total          | 30              | 100 | 30           | 100          |

change in Systolic and diastelic blood pressure while rise in blood pressure was observed in 60 percent of the patient. The rise in systolic blood pressure was in the range of 0-10 mm Hg in 27 percent of the patients, 10-20 mm Hg in 20 percent and 20-30 mm Hg in 13 percent of the patients. The rise in diastelic blood pressure was observed in the range of 0-10mm Hg in 30% of the patients, 10-20 mm Hg in 23% and 20-30 mm Hg in 7% of the patients (Table VII).

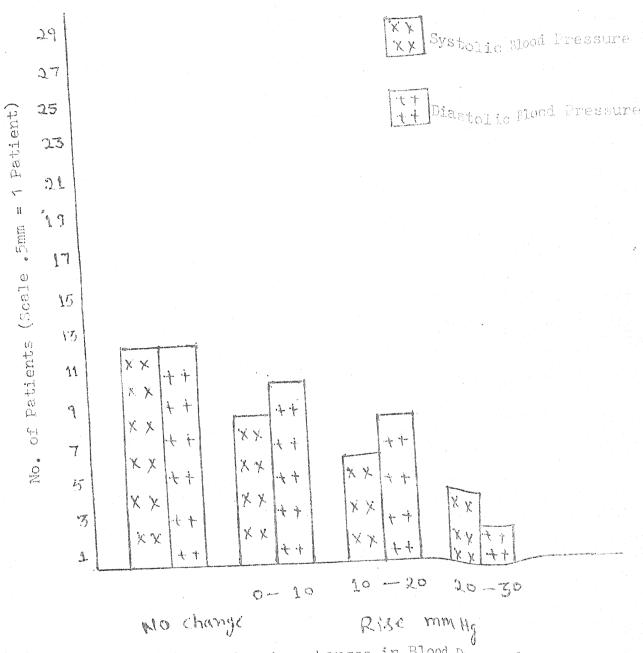


Diagram III - Showing changes in Blood Pressure, after administration of Pancuronium

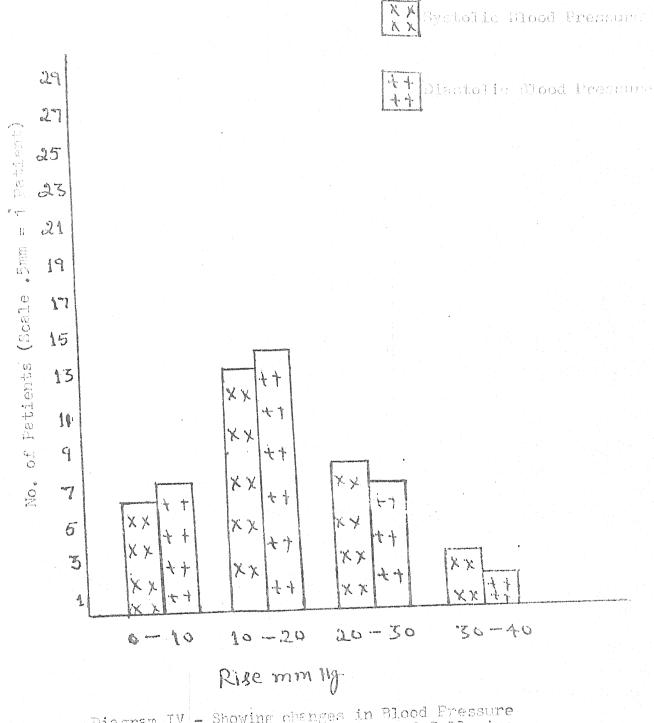


Diagram IV - Showing changes in Blood Pressure after administration of Gallamine

SABLE - 111
SHOWING THE CRANCE IN SLOOD PRESSURE RANGE FOULDWING THE

| Change in                    | Systolic Blood  | Propauro  | Diastolic Blood | ressure    |
|------------------------------|-----------------|-----------|-----------------|------------|
| Blood Pre-<br>saure<br>an Kg | No. of Patients | 3/4       | He.of Fatients  | <b>%</b>   |
| No change                    |                 | <b>60</b> |                 | <b>***</b> |
| Rise 0-10                    | 6               | 20        | 7               | 23         |
| R486 10-20                   | 13              | 43        | 14              | 4.7        |
| Rise 20=30                   |                 | 27        | 7               | 23         |
| R180 30-40                   | 3               | 10        | 2               | 7          |
|                              | . 30            | 100       | 30              | 100        |

Marked rise in blood pressure was recorded in all the patients of Gallamine group, Rise in systolic blood pressure was ranging from 0-10mm Hg in 25 percent of the patients, 10-20 mm Hg in 45 percent, 20-30 mm Hg in 27 percent and 30-40 mm Hg in 10 percent of the patients, while rise in diastolic blood pressure was in the range of 0-10 mm Hg in 23 percent of the patients, 10-20 mm Hg in 47 percent, 20-30 mm Hg in 23 percent and 30-40 mm Hg in 7 percent of the patients (Table VIII).

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DISCUSSION

employed drugs in the anaesthetic practice. It become possible to produced active muscular relaxation without unwanted effects on verious systems of the body, with the help of these drugs. Muscle relaxants are required during various surgical procedures particularly in the thoracic and abdominal operations. These agents also made it possible for the anaesthesiologist to have adequate required control over the ventilation of the patients.

The present study was profound to evaluate the efficacy of nondepolarising muscle relaxants.

Vecuronium, Pancuronium and Callamine on Cardiovascular system.

In the present study only adult patients
were selected. Their age ranged between 20 to 65
year to circumvent the variables at the extrema of
age. Fatients subjected to routine surgical precedures
were included in this study and emergency surgical

procedures were excluded to maintain standarised condition as for as possible. All patients were of ASA grade I or II.

type of premedication had no effects on dose requirement of relaxants, while Macdowell and Clarke (1969), Fandit and Dundee (1970), Magbagbeola (1972) administered a standard premedication. Atropine and Pethidine were used in this study as a premedication in all patients of each group. Ers. Bhargawa et al. (1977) also given Pethidine and Atropine as a premedication in their study.

In this study, same premedicant drugs, induction agents, and supplementary analgesis drugs were used in all cases to avoid the influence on the dosage and action of muscle relexant drugs.

found to most effective in possessing the Cardiovascular stability. The doses used in this study were recognized as being only approximately equipotent since most previous authors had found Vecuronium to be a little more potent than Fancuronium (Baird and Read 1960, Erieg, Crul and Booi; 1980, Vibymogensen, Jorganson

et al. 1980, Fahey et al. 1980 and herr et al (1982).

In this group 80% patient had no change in pulse rate. 83% and 87% of the patient had no change in systolic and diastolic blood pressure respectively, while only 20% patient showed slight rise (up to 10 beat/minute) in pulse rate. A little rise in systolic blood pressure was observed in 17% cases and 13% patient showed a minimal rise in diastolic blood pressure. These changes were not clinically significant. Our finding regarding heart rate and arterial blood pressure changes in fit adult patients after Vecuronium substantiate similar findings reported by other observers, Crul and Boolj (1980), Boolj et al. (1960), Gregoretti et al. (1982), Engback et al. (1983).

Bhatia et al. (1985), and Ferres et al. (1984).

Lavery et al. (1986) found that in healthy patients under carefully control condition, Vecuronium showed no significant changes in heart rate, systelic, diastolic and mean arterial blood pressure reduced significantly (P(0.05) 3-5 minute after Vecuronium administration. However by 30 minute the diastolic blood pressure was significantly greater than control. These occurs with Halothams anaesthesia Robertson et al.

in heart rate (4-5%) and was not considered clinically significant. The similar alteration was noted by Barnes et al. (1963). Animal experiment have shown that in contrast to Fancuronium and other nondepolarising muscle relaxants, Vecuronium in doses 20 times greater than these required for neuromuscular blockade, has no effect on the heart rate, arterial blood pressure or the sympathetic nervous system. Marshall et al. (1960), Fitzal et al. (1983). Agarwal et al. (1969) observed significantly elevation in mean pulse rate and mean arterial blood pressure during intubation which settled after 10 minute to a level above the preinduction level.

Vecuronium, being devoid of autonomic neural activities, does not produced any cardiovascular effects, Marshall et al. (1980), Booij et al (1980), Gregoretti et al. (1982) and Engback et al. (1983). Since Atropine was given before induction, patients had a tachycardia initially and consequently, the reasons for these changes in heart rate may be complex Rervik et al. (1988).

Considering the haemodynamic effects, the patients who received Fancuronium shows rise in pulse rate and blood pressure. The rise in pulse rate was the tune of 70%, while the blood pressure went up by

of the patients showed no change in pulse rate and blood pressure respectively. Slightly rise in blood pressure was observed in 30% of the patients while other 30% patients showed moderate rise in blood pressure. These results are comparable to the observation of Baird (1968), Mcdowell and Clark (1969) Levin (1971), Benett et al. (1973), Mrs. Bhargwa Enghack et al. (1983), Baijal et al. (1990) and Singh et al. 1990.

om heart rate and arterial blood pressure in man have been conflicting. Baird and Reid (1967) found that it had little effect on arterial blood pressure and heart rate, Modowell and Clark (1969) showed that it had little effect on heart rate and caused a slight, and statistically insignificant, fall of arterial blood pressure, conversely Loh (1970) found that in a dose of .12mg/kg. Pancuronium caused increases of both heart rate and mean arterial blood pressure.

Kelmen and Kemmedy (1971) observed that in a dose of 0.07mg/kg body weight, Pancuronium caused marked and statistically significant increase of heart rate accompanied by lesser, but still statistically significant

increases of mean arterial blood pressure. Barnes et al. (1982) showed that, when Pancuronium was used in clinical practice the tachycardia would be marked in the presence of vagal blockade and increase in mean arterial blood pressure did not appear to correlate with the increase of heart rate.

The most likely explanation for this discrepancy is that the cardiovascular actions of Pencureaium due to the release of Catecholamine Komesaroff (1970). The second concept is that it is secondary to the vagolytic action of the drug. Animal studies by Bonta, Gooriseen and Derkre (1968) suggested that Pencuronium reduces the effects of wagel stimulation on the heart, it might therefore be expected to cause on increase of heart rate, Duke et al. (1975) have shown that Pancuronius emerts its cardiovascular effects primarly by blocking muscarenic receptores in the heart, Bughes and Chapple (1976) proved in cats that Penguronium caused blocked at vagal post ganglionic sites in the heart an activity correlated well with the known liability of mild hypertension and tachycardia in man.

In the present study Gallamine was found to be most potent drug regarding to produced adverse effects over haemodynamic status of the patient.

of gallsmine triethiodide was marked in both degree and rapidity of onset, and in the present series the average increase in the rate was up to 40 beat per minute, which was accordance to Rennedy and Farman (1968). Tachycardia was said to occur however small the desage of Gallsmine triethiodide Doughty and Wylie (1951).

Marked rise in systolic and disstolic blood pressure was found following edministration of Gallamine. The maximum rise in blood pressure in the present series was up to 40mm Hg, which was comparable to Doughty and Wylle (1951), Kennedy and Farman (1968), Burnall et al. (1970), Eisele et al. (1971), Stoelting (1975).

in pulse rate in 32% and blood pressure in 36% of the patient while increases in pulse rate and blood pressure was recorded in 68% and 64% of the patient respectively.

Joshi and Ghesh (1981) have been observed me change in pulse rate in 14% of the patient while in 84% it was increased and 2% showed decrease in pulse rate. Fall in blood pressure was observed in 15%, me change in 36% and rises in 46% of the patient after administration of Gallamine.

tricthiodide has been believed to result from blockade of the muscarinic effects of acetylcheline liberated from the post gangtionic vagal nerve endings (Riker and Wescoe 1951). In this action, the drug resembles atropine, although it is much weaker (Laity and Garg 1962), but remarkably it exhibits this atropine like effect at no other site (Peton 1959). Neither is there any evidence of general sympathatic stimulation (Wein 1951) and the effects on Preganglionic sympathetic nerves are minimal (Millar and Biscoe 1965). A direct stimulant effect on intracardisc Bets receptors has been demonstrated (Morgenstern and Splinth 1965, Lee and Atkinson 1973).

Reversal with 12mg Atropine and 2.5mg Neestigmine was found to be adequate in all the cases in
three groups as judged clinically. Paired (1968) reported
that if reversal was attempted within 30 minute of the
Last dame, results were less than ideal in case of

a full paralysing dose of relaxant was still present at the end of operation, Gallamine in fact was more difficult to reverse with Meastigmine with equipetant dose of Pancuronium, Remson for this was beyond of explanation.

Baijal et al. (1990) was observed that 40% of the patient received Vecuronium, required no reversal.

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## CONCLUSION

From the present study we concluded that in comparision with Pancuronium and Gallamine, the Vecuronium represents a remarkable step toward the "Ideal muscle relaxant". Regarding Cardio-vascular stability.

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